



1225 Eye Street NW, Ste. 400  
Washington, DC 20005

September 8th, 2004

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Docket No. 2004N-0018, Federal Register: June 10, 2004 (Volume 69, Number 112, Pages 32467-32475)

Dear Sir/Madam:

The following comments are provided by the Biotechnology Industry Organization (BIO). BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products. BIO appreciates the opportunity to comment on the Food and Drug Administration's (FDA's, the Agency's) Proposed Rule on Human Subject Protection; Foreign Clinical Studies Not Conducted Under an Investigational New Drug Application.

### **General Comments**

BIO commends FDA for requiring adherence to the principles of Good Clinical Practice (GCP) for the conduct of clinical trials not conducted under an Investigational New Drug Application (IND) to be accepted as support for research and marketing applications. In 1997, FDA published in the Federal Register the International Conference on Harmonisation (ICH) Guidance document "Good Clinical Practice: Consolidated Guideline." The objective of this

ICH GCP Guidance is to provide a unified standard for the European Union (EU), Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

However, BIO is concerned that there will be confusion as to the specific GCP standard expected by FDA, as the GCP standard defined by FDA in this Proposed Rule contains some, but not all, of the requirements in the ICH GCP Guidance. For example, the Proposed Rule introduces a new or slightly modified definition of an Independent Ethics Committee (IEC) from that contained in the ICH GCP Guidance.

Because the ICH GCP Guidance already exists and has been adopted by FDA and used as guidance for industry since 1997, we would therefore like the following suggestions to be considered prior to finalization of the Rule:

- ?? BIO recommends FDA make specific reference to the ICH GCP Guidance in the Final Rule and require that foreign studies not conducted under an IND application follow the standards of GCP as documented in the ICH GCP Guidance document.
- ?? Alternatively, we would recommend that FDA acknowledge in the Final Rule, and/or in subsequent guidance, that the ICH GCP Guidance should be taken into account as one standard that FDA finds acceptable, and describe in what ways the standard presented in the revisions to 312.120 differs from the ICH GCP Guidance.

### **Specific Comments**

Recommendation #1: BIO notes that FDA considers the GCP standard in proposed section 312.120 to be consistent with the ICH GCP standard. However, we believe critical elements are missing and recommend the following requirements be included in the Final Rule:

- ?? Requirements for record keeping by investigators (as specified as Essential Documents under ICH and comparable to 312.62 under FDA IND regulations).
- ?? Requirement that sponsors obtain written commitments from investigators to comply with GCP and the study protocol.
- ?? We recommend the requirement in section 312.120(b) (7) of the Proposed Rule on documenting IEC decisions also account for documenting continuing review by the IEC, which is a critical element noted under section 312.120 (a) (1) (i) of the Proposed Rule.

Recommendation #2: Currently section 312.120 (c) (1) allows for the demonstration that clinical research was conducted according to the laws and regulations in a country where such laws provide for greater protection of human research subjects than the principles of the Declaration

of Helsinki. BIO recommends that FDA include in the revisions to 312.120 a provision to continue to allow a sponsor to document that a study was conducted in a country where the laws and regulations already provide for strict adherence to the principles of GCP, which would clearly provide for the assurance of protection of human research subjects and the quality of clinical data. For example, clinical trials conducted in Europe must now meet the requirements of the EU Clinical Trial Directive and its implementing guidance for the conduct of clinical trials under GCP.

Recommendation #3: In section 312.120 (b) (6), the Proposed Rule requires that the "names and qualifications for the members of the IEC that reviewed the study" be submitted as supporting information. BIO has two recommendations on this provision.

- ?? For trials conducted in Europe, confidentiality issues and restrictions on the transfers of data may exist due to provisions of EU data protection laws. BIO recommends changing this requirement to "Information on the composition (preferably names and qualifications, but at a minimum qualifications) of the IEC that reviewed the study to ensure that the IEC is duly constituted".
- ?? Furthermore, BIO recommends that FDA provide clarification on the types of information that must be provided to document the qualifications of IEC.

In conclusion, we appreciate the opportunity to provide our comments and look forward to finalization of the Proposed Rule.

Sincerely,

A handwritten signature in cursive script that reads "Sara Radcliffe".

Sara Radcliffe  
Managing Director  
Science and Regulatory Affairs